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Chemical Nature of Cibulins—Induced Fungitoxic Substances from Onion

18400212 Kiev DOKLADY AKADEMII NAUK UKRAINSKOY SSR. SERIYA B: GEOLOGICHESKIYE, KHIMICHESKIYE I BIOLOGICHESKIYE NAUKI in Russian No 11, Nov 87 (manuscript received 14 Apr 87) pp 70-74

[Article by A. P. Dmitriyev, L. A. Tverskoy, A. M. Kolesnikov, A. V. Kovtun and D. M. Grodzinskiy, corresponding member, UkSSR Academy of Sciences, Institute of Botany, UkSSR Academy of Sciences; Institute of Organic Chemistry, UkSSR Academy of Sciences]

[Abstract] Results of study of the chemical structure of induced fungitoxic substances from the onion, called cibulins, were described and discussed. The qualitative composition of cibulins in healthy and necrotic onion tissue was identical and no significant differences in qualitative composition of cibulins between different varieties of onions were found. Examination of the chemical structure of the cibulins by elemental analysis and IR, UV and paramagnetic resonance spectra of mixtures of them and individual fractions showed the cibulins to be sulfoxide-containing organic acids with a C_3H_7-SO-R structure, where R is not an alanine residue but a long-chain fatty acid with varying chain length, isomerism and position of unsaturated double bonds. Figures 4; references 9 (Russian).

02791

Organic Synthesis, Biocatalysis and New-Generation Drugs

18400309 Moscow ADVANCES OF SCIENCE AND TECHNOLOGY in English No 35, 15 Dec 87 pp 1-6

[Article by Svetlana Vinokurova, APN science news analyst]

[Text] "Biocatalysis in fine organic synthesis is just taking its first steps. However, the extensive search for new enzymes, genetic engineering and the breakthroughs in the fundamental studies into the laws of enzymatic reactions together with existing approaches such as the stabilization and immobilization of enzymes allow the assertion that we are at the threshold of the development of new biocatalytic technologies for modern industry."

Such is the view of Vitas Sviadas, a leading researcher with the A. Belozerskiy Interfaculty Laboratory of Molecular Biology and Biorganic Chemistry at Moscow State University and a USSR State Prize-winner for 1984.

Organic synthesis is generally regarded as the pinnacle of chemistry. Like no other field of science, here the leading role is often played by the researcher's intuition, so fine organic synthesis is, to a certain extent, akin to art. However, with the accumulation of new knowledge, that sphere too is getting on the hard soil of preset tasks and their accomplishment with the use of proven tools, so to speak. This fully applies to biocatalysis whose sphere of application is becoming broader all the time. The unique ability of natural biocatalysts or enzymes to act selectively and specifically under "mild conditions" at a high speed and without side reactions has made biocatalysis first attractive and then highly promising from the technological point of view. They are used in the production of drugs, amino acids, peptides, certain organic acids, tagged compounds and agents for research purposes and so on.

However, at the very start biocatalysis ran into major difficulties. To develop a technology, it is necessary to find an enzyme with specific characteristics, to study the properties of the base substance and its possible transformation, to figure out the factors of the reaction's effectiveness and to design a technological catalyst suitable for mass production on the basis of that enzyme. It is exactly because of these difficulties that the number of accomplished catalytic processes is quite limited: in practice hydrolytic enzymes have found the broadest application so far, especially in the field of modifications of antibiotics such as penicillins and cephalosporins.

The Nobel Prize winner in chemistry Woodworth called penicillin a challenge to the organic synthesis chemists of the 20th century. Indeed, both synthesis and modifications of antibiotics are monumental tasks. They involve a whole series of extra-fine chemical manipulations. Take, for example, the removal of a side radical in an antibiotic molecule. In other words, it is a multi-stage, energy-intensive process.

Biocatalysis for the production of the key element of the synthesis of new penicillins began to be used in the Soviet Union and in the world in the mid-70s. Soviet engineers developed the first engineering enzymology process in that field. In other words, it was the beginning of the era of engineering uses of enzymes. The new process was developed due to a lucky symbiosis of fundamental research, applied science and efforts by the medical industry. The whole cycle from the development to the introduction of the new technology took the experts of the All-Union Research Institute of Antibiotics of Moscow State University, Tallinn Polytechnic and the chemical plants in Riga and Saransk about 5 years. The transition to the new technology appreciably simplified the process, increasing the product yield and the general production volume. In 5 years it saved dozens of millions of rubles in nationwide terms. This resulted in an increased output of semi-synthetic penicillins and a drop in their production costs.

In the same manner—i.e., through the use of an immobilized penicillin amidase—Soviet biologists developed the second process of engineering enzymology: the separation of the key compound for the synthesis of new cephalosporins. As it turned out later, this enzyme can help synthesize such antibiotics as cephaloxin, cephalotin, and cephaloridin. Today, experts are studying the opportunities for enzymatic synthesis of a whole range of other antibiotics. In 1984, the work carried out under the supervision of Professor Sergei Navashin was awarded a USSR State Prize.

One should also mention the ever growing importance of obtaining optically pure amino acids in modern biotechnology for medical and food industries, livestock breeding and science. A chemical solution in this case is very difficult, but not impossible.

One possible way out is biocatalytic conversion of derived amino acids into optical isomers or enantiomers. As a result, one can obtain a mixture of one unreacted antipode with another modified antipode which can be easily separated. Since, as a rule, the rates of enzymatic cleavage of the enantiomers differ very strongly, such cleavage helps obtain amino acid enantiomers of extraordinary high optical purity, and extra-pure substances admittedly have many advantages and a high value.

The instruments of cleavage for derived amino acids are common enzymes which can be found in animals, plants, and microorganisms. This can also be done with the help of proteolytic enzymes which are highly stereospecific. Still another way is the conversion into amino acids of certain derivatives whose chemical synthesis is relatively easy. In other words, the task of obtaining optically pure

amino acids has evoked a whole series of solutions. The latter solution, for example, can be used in the production of the essential amino acid lysine.

"An interesting example of the use of biocatalysis in pharmacology is the enzymatic transformation of arachidonic acid with the subsequent release of prostaglandins, thromboxanes, prostacyclin, and leukotrienes. At extralow concentrations, these intracellular regulators ensure powerful physiological responses of the organism," says Vitas Sviadas, returning to the subject of drugs. "Prostaglandins are already being used, and prostacyclin and leukotrienes will certainly be used in such fields of medicine as gynecology, bronchial asthma treatment, gastroenterology, blood pressure regulation, treatment of cardiovascular diseases, and so on. Prostaglandins are also already playing an important role in commercial livestock breeding.

The conversion of arachidonic acid into prostaglandins is catalyzed by complex systems which have a common key enzyme. This notably results in coupled oxidation by oxygen of arachidonic acid and some electron donors, where the donors may be weak inorganic or organic reductants like adrenaline or tryptophan. In the way of these remarkable transformations which are so vital for man, though, stands another barrier: the intermediate product of catalysis, one of the prostaglandins, is at the same time a powerful inactivator of the enzyme which forms it.

The paradox in the curse of the enzymatic reaction with the enzyme's self-destruction has long attracted the attention of world science. Experiments staged under the supervision of Professor Sergei Varfolomeyev of Moscow State University have shown that this mechanism has a considerable physiological meaning, since it helps maintain a constant level of concentration of these physiologically active substances in living systems. The discovery of the mechanism of the enzyme's inactivation gives scientists the hope of choice of the conditions under which it is used and which ensure a maximum yield of the wanted substance with a minimal loss of the biocatalyst.

All this, however, is just a fragment of the overall problem of biocatalytic conversion of arachidonic acid into prostaglandins and thromboxanes: an interesting but certainly not all-embracing factor. One should also mention the association with the enzyme which determines the pattern of the transformation of the intermediate compound into, say, leukotrienes, which are of very great interest for medicine. They play an important role in rehabilitation processes and in the course of such diseases as bronchial asthma and others.

Today, scientists are studying the physiological role of all the enzyme transformations of the arachidonic acid cascade. They are trying to single out the key compounds which will have the greatest clinical importance. That, however, will call for the development of effective technologies for the production of new drugs.

Despite all the difficulties in the designing of biocatalytic processes in this field, there is every reason to believe that the natural multienzyme systems of arachidonic acid transformations can serve as a basis for the development of catalysts of biotechnological processes. I might also note here that the basic product of all these transformations, arachidonic acid, can be obtained from suitable oils by way of biocatalysis with the use of specific enzymes.

"The ultimate goal of enzymatic synthesis," Vitas Sviadas continues, "is maximum yield of the desired product. Besides such important factors as the specificity of the biocatalyst and the thermodynamic and kinetic characteristics of the reactions involved, a great deal depends on the choice of the way of increasing the product yield. For example, low solubility of the substance being synthesized and its sedimentation ability may govern the terms of that synthesis. The reaction becomes perpetual when one of its products gets involved in a follow-up thermodynamic reaction. The recovery of the desired product in a number of systems may depend on the accuracy of the calculation of the time of contact between the reaction mixture and the biocatalyst. This is because the important thing here is not to miss the peak when the continuation of enzymatic transformations in a water medium becomes unprofitable thermodynamically. Much more promising in this sense is biocatalysis in water-organic mixtures, including those made up of water and water-insoluble organic solvents. Experiments by the group of Professor Karel Martinek of Moscow State University have shown that in such systems the number of attainable changes in the balance constants runs into tens of thousands.

This approach is being used now in the synthesis of peptides, which allows modifications in such poorly soluble substances as, say, steroids. In other words, the road to biocatalysis in fine organic synthesis has been found, which allows one to hope for the development of new biocatalytic technologies in modern industry.

/09599

Study of Hydration of Neurosporin and Trivalent Iron Complex

18400213 Kiev TEORETICHESKAYA I EKSPERIMENTALNAYA KHIMIYA in Russian Vol 23, No 6, Nov-Dec 87 (manuscript received 10 Oct 86) pp 680-686

[Article by V. Ye. Khutorskiy, A. A. Kamenchuk and A. M. Nesterenko, Institute of Organic Chemistry, UkSSR Academy of Sciences, Kiev]

[Abstract] The electron structure and hydration of a complex of neurosporin (a hydroxamine type of siderophore of the fusarinine family) and trivalent iron were

studied by the PPDP/2 and Monte Carlo methods. The Fe atom contain a small positive charge. The hydrate shell of the complex is asymmetric, especially in the area of ligand groups, each of which binds one water molecule. Hydration of the remaining polar groups binding with one or two molecules of water is extremely important. The results of calculations of the free energy of hydration of neurosporin and its separate groups of atoms were presented and discussed. A molecular model of transport of the complex was described. The predominance of the role of polar groups of neurosporin in determining the free energy of hydration was confirmed, which helped to explain the specific nature of its membrane action. Figures 4; references 16: 2 Russian; 14 Western.

02791

Some Biological Properties of Synthetic 11-Desoxy-E and 11-Desoxy-F-Alpha Prostanoids

18400214a VESTSI AKADEMII NAVUK BSSR: SERYYA KHIMICHNYKH NAVUK in Russian No 6, Nov-Dec 87 (manuscript received 2 Jul 87) pp 72-76

[Article by B. B. Kuzmitskiy, M. B. Golubeva, I. G. Dadkov, N. A. Mizulo, V. N. Romanova, G. A. Shafranskaya, A. Ye. Golikov, Ye. V. Koroleva, T. V. Yankova and F. A. Lakhvich, Institute of Biorganic Chemistry, BSSR Academy of Sciences]

[Abstract] A study of the biological properties of seven prostaglandins of the 11-desoxy-E_1, -E_2 and -F_{alpha} series and their precursors was described and discussed. The protective effect of the compounds on the gastric mucosa was studied in experiments on female Wistar rats (190-230 g) which fasted for 24 hours. Destruction of the gastric mucosa, caused by ligation of the pylorus for 5-6 hours, was assessed macroscopically. Doses of the compounds ranged from 1-20 μg/kg of weight or 5 μg/kg for a single injection of the most effective dose. The 5 μg/kg dose of the prostanoids produced an anti-ulcerative effect and prevented 55-75 percent of the destruction of the stomach wall in comparison with the control animals. The cytoprotective effect of the compounds did not depend on their structural features and was dose-dependent for only two of the compounds. Four of the prostanoids inhibited local inflammation and two stimulated it. The different effect of the compounds on experimental edema, vascular permeability and erosion of the gastric mucosa made it difficult to choose the best prostanoid as an anti-ulcer compound. The compounds did not affect the immune system or tumor growth. References 15: 4 Russian; 11 Western.

02791

Total Synthesis and Properties of Prostaglandins. XIII. Synthesis of Some 11-Alkyl-Substituted 11-Desoxyprostaglandins E

18400214b Riga IZVESTIYA AKADEMII NAUK LATVIYSKOY SSR: SERIYA KHIMICHESKAYA in Russian No 6, Nov-Dec 87 (manuscript received 18 Dec 86) pp 731-739

[Article by V. R. Korits, S. Kh. Rozite, Ya. F. Freymanis and G. P. Sokolov, Institute of Organic Synthesis, Latvian SSR Academy of Sciences]

[Abstract] Derivatives of E and F series prostaglandins with alkyl substituents at C-11 are more resistant to the effect of chemical and biological factors than are the parent compounds with a C-11 hydroxyl group. One method of producing these derivatives is the coupled 1,4-addition of nucleophiles to derivatives of type A prostaglandins. This article describes the synthesis of 11-carbon-substituted 11-desoxyprostaglandins E by coupled 1,4-addition of an n-butyl or trimethylsilylmethyl group to series A prostaglandins using the cuprate method. The starting compounds were 2-methoxycarbonylmethyl - 3 - (tetrahydrofuranyloxy - trans-oct-1-enyl)cyclopent-4-en-1-one (α and β isomers), 2-(6-methoxycarbonylmethylhexyl)-3-(3-tetrahydrofuranyloxy trans-oct-1-enyl)cyclopent-4-en-1-one (α and β isomers), and 2-(6-methoxycarbonyl-cis-hex-2-enyl)-3-(3-tetrahydrofuranyloxy-trans-oct-1-enyl)cyclopent- 4 - en - 1 -one. After the addition reaction, the protective tetrahydrofuranyl group at position 15 was removed, giving the 11-substituted methyl esters. Saponification gave the corresponding acids. Mass spectra of the compounds were obtained. References 14: 6 Russian; 8 Western.

02791

Copper-Dependent Site-Specific "Self-Cleavage" of Single-Stranded DNA in Presence of Ascorbate and Hydrogen Peroxide

18400235b Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 298, No 4, Feb 88 (manuscript received 20 Jul 87) pp 1011-1015

[Article by T. G. Astashkina, V. V. Vlasov, S. A. Kazakov and S. V. Mamayev, Novosibirsk Institute of Bioorganic Chemistry, Siberian Department of USSR Academy of Sciences]

[Abstract] Transition metal ions are capable of catalyzing site-specific cleavage of RNA. In this paper copper-dependent, self-cleavage of single-stranded DNA was shown to occur in a site-specific manner in the presence of ascorbate and H_2O_2. Single-stranded DNA labeled with ^{32}P at the 3'-terminus was studied; it corresponded to one of the RNA fragments of tick encephalitis virus (teDNA). This site-specific cleavage did not occur in the presence of ascorbate or H_2O_2 alone. None of the other biologically active metals studied produced this phenomenon. Preincubation of teDNA with ethylene diamine tetraacetic acid (EDTA), which has high affinity

towards Cu ions, inhibited this cleavage of DNA. 1,1'-o-Phenanthroline increased the rate of this cleavage, which occurred at position G143. Both the acceleration and inhibition of this process are related to complex formation with phenanthroline and copper ions. This cleavage is not a unique property of a particular nucleic acid and could take place with many DNA's. Figures 3; references 15: 1 Russian, 14 Western.

7813/9604

Functional Segments of Gamma-Subunit of 3',5'-GMP Phosphodiesterase from External Segments of Retina Rods: Evaluation Based on Monoclonal Antibodies

18400235c Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 298, No 4, Feb 88 (manuscript received 24 Jun 87) pp 1019-1021

[Article by I. L. Dumler, N. O. Artemyev, T. D. Chernova and R. N. Etingof, Institute of Evolutional Physiology and Biochemistry imeni I. M. Sechenov, USSR Academy of Sciences, Leningrad]

[Abstract] The γ-subunit of 3',5'-GMP phosphodiesterase (PDE) of the retina photoreceptor membrane plays a key role in development of photoreception. During adaptation to darkness it inhibits PDE; upon illumination the inhibition is switched off, activating PDE. The switching off process is initiated by the α-subunit of transducin, the GTP-binding protein of the photoreceptor cell. The mechanism of the interaction of this protein with the γ-subunit of PDE is not clear. In the present work various functional segments of the PDE inhibitor molecule were evaluated using monoclonal antibodies. Analysis of the data obtained showed high specificity of individual segments of the PDE inhibitor molecule: interaction of this molecule with individual proteins occurs at different segments of the molecule. The segment of the γ-subunit which interacts with the catalytic subunits of PDE and thereby provides inhibition was unaffected by antibodies, whereas the photoinduced PDE activation was blocked by antibodies. Figures 2; references 13: 5 Russian, 8 Western (1 by Russian authors) 7813/9604

Determination of DNA-Protein Binding Constants Using a Computer-Linked Chromatography System

18400236c Kiev BIOPOLIMERY I KLETKA in Russian Vol 4, No 1, Jan-Feb 88 (manuscript received 30 Jun 86) pp 20-27

[Article by Yu. A. Kalambet, Ye. I. Burova, A. A. Zhuchkov, V. L. Knorre and A. A. Aleksandrov, Institute of Molecular Genetics, USSR Academy of Sciences]

[Abstract] Several methods exist for determination of DNA-protein binding constants based on gel chromatography. In all of them the crucial problem is that DNA and protein concentrations as a function of time cannot be obtained concurrently. Combining a Milikhrom multiwavelength scanning chromatograph with an Iskra-226 on-line computer made it possible to register DNA and protein concentrations at any moment. The DNA and protein concentrations as a function of time can then be used to determine DNA-protein binding constants. The results obtained with such a system were described for the binding of Escherichia coli RNA polymerase with plasmids pA03, pUC19 and pBR322 containing the growth hormone gene as well as with single-stranded oligodeoxyribonucleotide sequences—fragments of E. coli spc and trpR gene promoters. References 19: 1 Russian, 18 Western (5 by Russian authors).

7813/9604

High Performance Liquid Chromatography of Synthetic Prostaglandin E Analogs

18400237b Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 13, No 10, Oct 87 (manuscript received 24 Oct 86, after final revision 4 Mar 87) pp 1416-1421

[Article by N. K. Levchenko, I. V. Torgov, M. S. Miftakhov and G. A. Tolstikov, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow; Institute of Chemistry, Bashkir Affiliate of USSR Academy of Sciences, Ufa]

[Abstract] Preparative high performance liquid chromatography (HPLC) of synthetic prostaglandin E was reported, including removal of impurities and separation of the α and β C-8 isomers and 15-OH epimers. Separation of their synthetic precursors, the leukotrienes, was achieved with a 98-99 percent degree of purity. On the basis of the results obtained, recommendations were made for preparative HPLC of synthetic prostaglandins on a scale of up to 300 mg. Figures 6; references 7: 1 Russian , 6 Western.

7813/9604

Automated Synthesis of Oligodesoxyribonucleotides. VI. Investigation of Cellulose-Based Segmental Supports

18400237a Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 13, No 10, Oct 87 (manuscript received 26 Nov 86, after final revision 27 Feb 87) pp 1358-1365

[Article by A. I. Lomakin and S. G. Popov, All Union Scientific Research Institute of Molecular Biology, Koltsovo, Novosibirsk Oblast]

[Abstract] One of the most promising methods of chemical synthesis of DNA fragments is their simultaneous synthesis on segmental carriers (paper disks). A large number of oligomers up to 20 bases long can be obtained in a short time period using the segmental approach. Recently it was shown that this originally manual procedure could be automated. One important step in developing this procedure is the evaluation of various cellulose materials for supports. Some of the results of these evaluations have now been reported. Using Whatman and Filtrak chromatographic papers, it was shown that mild acid or base treatment of paper disks led to consid-

erable increase of cellulose reactivity. Segmental carriers from cellulose fibers (flax or cotton) are much stronger than paper, can be washed much easier and are adaptable to automated procedures. The yield on cellulose fibers was comparable to that on paper disks. Figure 1; references 14: 9 Russian, 5 Western.

7813/9604

ATP Level in Synaptosomes as a Determining Factor of Functional Activity of Ionic Channels Induced by Alpha-Latrotoxin

18400245 Kiev UKRAINSKIY BIOKHIMICHESKIY ZHURNAL in Russian Vol 60, No 1, Jan-Feb 88 (manuscript received 5 May 87) pp 65-69

[Article by T. A. Pivneva, N. G. Gimmelreykh and Ye. V. Nikolishina, Institute of Biochemistry imeni A. V. Palladin, UkSSR Academy of Sciences]

[Abstract] This study had two goals: first, to investigate the relationship between α-latrotoxin-induced calcium fluxes and the level of cytoplasmic ATP in the synaptosomes; and second, to investigate the effect of agents which change ATP levels on these toxin-induced calcium channels. It was shown that incubation of synaptosomes with glucose and monoiodoacetate lowered the level of ATP and inactivated α-latrotoxin-induced calcium flux. Introduction of succinate or pyruvate into the medium increased ATP levels in synaptosomes and this was accompanied by a significant increase in the effect of α-latrotoxin on $^{45}Ca^{2+}$ influx into synaptosomes. Treatment of synaptosomes with theophilline and caffeine had no effect on basal calcium permeability, but papaverine lowered the effect of α-latrotoxin. Figures 3; references 12: 7 Russian, 5 Western.

7813/9604

Effect of Lipid Peroxidation on Disk Membrane Photoreceptor Conductivity

18400197a Yerevan NEYROKHIMIYA in Russian Vol 6, No 3, Jul-Sep 87 (manuscript received 7 Jan 87) pp 413-417

[Article by T. I. Rebrik, G. R. Kalamkarov and M. A. Ostrovskiy, Institute of Chemical Physics, USSR Academy of Sciences, Moscow]

[Abstract] The photoreceptor membrane contains a very high level of polyunsaturated fatty acids which makes it readily subject to peroxidation. It has also been observed that a bright flash of light with intensity significantly above the physiological level causes a rapid increase of disk membrane conductivity. A study was performed in order to determine whether or not such an increase of photoconductivty is associated with photooxidation of molecular components of the membrane. Outer segments of bull rods were used in the study. Lipid photooxidation did not cause the rapid increase of photoreceptor disk membrane conductivity in response to light. Lipid peroxidation increased photoreceptor membrane conductivity after accumulation of much larger amounts of products of oxidation. Regeneration of rhodopsin in bleached disks with addition of 11-cis-retinal restored the amplitude of photoresponse and decreased photoreceptor conductivity. It was assumed that photoinduced increase of disk membrane conductivity is associated with conformational changes of the rhodopsin molecule or disruptions in rhodopsin interaction with lipids. Figures 3; references 6: 4 Russian; 2 Western.

02791

Transfectomas, Producers of Artificial Antibodies

18400194a Moscow BIOTEKHNOLOGIYA in Russian Vol 3, No 6, Nov-Dec 87 (manuscript received 24 Apr 87) pp 796-801

[Article by S. M. Deyev and O. L. Polyanovskiy, Institute of Molecular Biology, USSR Academy of Sciences, Moscow]

[Abstract] Recently, monoclonal antibodies of varying specificity have been used mainly for diagnostic purposes but also for the purpose of purifying and binding different antigens. However, their use in therapy and diagnosis in situ is limited by the fact that molecules of mouse immunoglobulins cause a more or less potent immune response in man which is dangerous for patients and which causes binding of allogenic mouse antibodies. The use of human monoclonal antibodies is limited because of their scarcity, instability of cell lines and low yield. Now it is possible to create artificial antibodies. This is confirmed by data in the literature which show that a combination of genetic engineering and cell engineering permits synthesis of genes of artificial antibodies and creation of cells, transfectomas, which produce the corresponding antibodies. Two main trends of the process are being developed: production of recombinant antibody genes (mouse/man) and genes which encode bifunctional molecules. Tranfectomas which produce antibodies to specific tumor antigens are being created. It has been proposed that they be used for both diagnostic purposes and for cancer therapy. Figures 3; references 23: 2 Russian; 21 Western.

02791

Scale-up of Biochemical Recirculating Column Reactor Based on Complete Mathematical Model of Biosynthesis Process

18400216 Ivanovo KHIMIYA I KHIMICHESKAYA TEKHNOLOGIYA in Russian Vol 30, No 10, Oct 87 (manuscriptreceived31Jan87)pp 101-106

[Article by A. D. Krumov, L. S. Gordeyev and A. Yu. Vinarov, Moscow Chemical Technological Institute imeni D. I. Mendeleyev; All-Union Scientific Research Institute of Protein Synthesis; Department of Cybernetics of Chemical Technological Processes]

[Abstract] Scale-up of a column biochemical reactor required development of a complete mathematical model of the process of accumulation of biomass proceeding in it with consideration of the kinetics of microbiological synthesis, mass transfer and heat transfer and structure of flows of heat and gas phases in the bioreactor. The model includes equations of material balance for microorganisms and carbon-containing substrate in the culture fluid and for oxygen and carbon dioxide gas and heat balance equations. A block-diagram of the algorithm of optimization of design and technological parameters of the industrial bioreactor was presented and discussed. Basic optimal characteristics of the model device and an industrial reactor were compared. Figures 2; references 6 (Russian).

02791

Immunochemical Features of Cholera Enterotoxin Subunits and Thermolabile Enterotoxins of E. Coli of Different Origin

18400195c Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 10, Oct 87 (manuscript received 20 Feb 87) pp 472-475

[Article by S. Ye. Voronov, Yu. V. Vertiyev, I. A. Shaginyan and Yu. V. Yezepchuk, Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamalaya, USSR Academy of Medical Sciences, Moscow]

[Abstract] A comparative immunochemical analysis of subunits A and B of cholera enterotoxin and thermolabile enterotoxins from human E. coli strain [hLT] and thermolabile enterotoxins from swine E. coli strain [pLT] was performed by use of double immunodiffusion on agar gel in order to determine related and individual antigenic determinants of each of the subunit proteins. Nine types of antigenic determinants, isolated from different sources, appeared in subunits of the cholera enterotoxins and the thermolabile E. coli enterotoxins which were grouped as follows: in subunits B, 1) antigenic determinants common for subunits B of all 3 enterotoxins—B(chp); 2) group antigenic determinants common for subunits B of 2 toxins in pairs—B(ch), B(hp); 3) individual antigenic determinants—B(c), B(h), B(p); in subunits A, 1) antigenic determinants common for all 3 enterotoxins—A(chp); 2) group antigenic determinants common for A subunits of 2 enterotoxins (hLT and pLT)—A(hp); 3) individual antigenic determinants—A(c). The antigenic structure for subunits of the three related enterotoxins was given on the basis of these findings. These antigenic determinants may be included in immunoprophylactic preparations and may be used to construct immunodiagnostic test systems. Figures 3; references 14 (Western).

02791

Critical (Percolation) Behavior and Fractal Dimensions of Aggregates in Immunological Agglutination Reaction

18400236b Kiev BIOPOLIMERY I KLETKA in Russian Vol 4, No 1, Jan-Feb 88 (manuscript received 26 Jun 86) pp 35-40

[Article by V. A. Markel and M. I. Shtokman, Institute of Automation and Electrometry, Siberian Department of USSR Academy of Sciences, Novosibirsk; Novosibirsk State University]

[Abstract] Kinetic and equilibrium characteristics of the agglutination reaction were analyzed on a theoretical basis. Experimental data obtained in another study by other authors (I. G. Yersh, L. S. Muratov, S. Yu. Novozhilov et al., DOKLADY AKADEMII NAUK SSSR, Vol 287, No 5, 1986, pp 1239-1244), in which the kinetics of agglutination of Yersinia pestis bacteria were studied by laser correlation spectroscopy, have been interpreted and restated. These equilibrium and kinetic properties were analyzed from the standpoint of the physical theory of phase transitions and scale invariance (static and dynamic scaling). A percolation model was proposed for a quasi-agglutination reaction which predicts the critical behavior of the reaction as a function of the concentration of serum. Appearance of a cluster of agglutinated particles was shown to be similar to a second-order phase transition. The kinetics of the early stage of the agglutination reaction corresponded to the predictions of dynamic scaling. This approach permits determination of fractral dimensions of bacterial clusters, which were shown to be distinct from the spatial dimensions. Figures 3; references 12: 3 Russian, 9 Western.

7813/9604

Immunochemical Method of Determining Antigenic Contamination of Environment

18400209 Moscow GIGIYENA I SANITARIYA in Russian No 11, Nov 87 (manuscript received 23 Jul 86) pp 40-43

[Article by S. V. Lebedev, V. P. Chekhonin and A. V. Prygun]

[Abstract] A method of determining antigenic contamination of the environment by means of immunochemical identification of antigens with the aid of heterogeneous antibodies is described and discussed. Some methods based on antigen-antibody reactions which fulfill the requirements for high specificity and resolving capacity and practical accessibility were discussed briefly. A block diagram of the procedure for monitoring contamination of the environment is presented and discussed. The method was used to assess contamination of the external environment by antigens associated with air conditioning and ventilation systems. These antigens, apparently of microorganism origin, accumulate in dust, water and sludge in different parts of air conditioning and ventilation systems and are associated with some exogenic, allergic alveolites. Figures 2; references 13: 9 Russian; 4 Western.

02791

Acceleration of Retrograde Axoplasma Flow by Laser Irradiation

18400204a Frunze ZDRAVOOKHRANENIYE KIRGIZII in Russian No 6, Nov-Dec 87 pp 23-26

[Article by B. Sh. Usupbekova, Alma-Ata State Medical Institute]

[Abstract] Treatment of patients with nerve damage depends on the solution of important theoretical problems related to acceleration of regeneration of nervous system structural elements. A new method has recently appeared for evaluation of the restoration of connections between neurons, based on retrograde axonal transport of the enzyme horseradish peroxidase. This article studies the influence of low-energy laser radiation on retrograde axoplasma flow processes in the regenerated fibers of the cervical segment of a sympathetic nerve trunk, using the peroxidase method for this purpose for the first time. The experiments, performed on 40 cats, indicated that low-intensity laser radiation accelerated retrograde axoplasma flow by 20% during the post-traumatic period following surgical cutting of nerve fibers. Figures 5.

06508

Electron Microscopic and Radioautographic Investigation of Bronchi in Chronic Inflammation Upon Exposure to Helium-Neon Laser

18400234d Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 12, Dec 87 (manuscript received 3 Apr 87) pp 743-749

[Article by L. M. Nepomnyashchikh, V. V. Polosukhin, G. I. Nepomnyashchikh and V. P. Tumanov, Laboratory of Ultrastructural Pathology, Division of Pathomorphology and Morphometry, Institute of Clinical and Experimental Medicine, Siberian Department of USSR Academy of Medical Sciences, Novosibirsk; Laboratory of Histochemistry and Radioautography, Division of Pathological Anatomy, Institute of Surgery imeni A. V. Vishnevskiy, USSR Academy of Medical Sciences, Moscow]

[Abstract] Because of the fact that the mechanism of laser biostimulation is virtually unknown, its clinical application is empirical in most cases. Structural and metabolic changes in the bronchial mucosa of patients with chronic inflammatory processes were investigated during helium-neon laser therapy of 39 men, 28-62 years old, with chronic suppurative lung diseases. The overall morphological presentation of the biopsied mucuous membrane corresponded to chronic bronchitis with cilium reduction and metaplasia of cylindrical epithelium into a flat multilayered structure. Marked changes were observed both in the epithelium and in the underlying stroma of bronchi after 5-8 days of laser therapy. The structural changes were described in detail. Radioautographic study showed intensified metabolic activity during this period. The principal phenomenon occurring during laser therapy is hyperplastic transformation with heterotrophy of bronchial epithelium and corresponding rebuilding of the underlying connective tissue. Figures 3; references 15: 12 Russian, 3 Western.

7813/9604

Laser Radiation: Effect on Drug Distribution in Ocular Tissue (Experimental Study). Communication 1

18400247 Moscow VESTNIK OFTALMOLOGII in Russian Vol 104, No 1, Jan-Feb 88 (manuscript received 9 Dec 86) pp 40-42

[Article by G. A. Kiselev, O. I. Lebedev, V. S. Pospelov and A. V. Lukoshkin, Department of Eye Diseases (headed by Professor G. A. Kiselev) and Central Scientific Research Laboratory (headed by V. V. Lobov), Omsk Medical Institute]

[Abstract] Improved effectiveness of eye medications may be achieved by a method of administration which assures their high concentration in target tissues. The goal of this study was to evaluate increased effectiveness of various eye medications used in conjunction with laser beam irradiation. Experiments were performed on rabbits. It was shown that irradiation with an LGN-105 helium-neon laser (2 mW) for 10 minutes significantly enhanced diffusion of medicinal preparations within agar gels and led to at least a 50 percent increase of their content in the eye tissue. The maximal increase of the concentration of medicines occurred in the vitreous body. References 13: (Russian).

7813/9604

Contaktins Reduce Tumor Incidence in Animals

18400310 Moscow ADVANCES OF SCIENCE AND TECHNOLOGY in English No 3, 25 Jan 88 pp 1-5

[Text] Can old age be delayed? Yes, it can, say experts, provided a solution is found for the problem of extending man's life. What does modern medical science propose for it?

Among the many trends is a fundamentally new method of eliminating hereditary predisposition to various diseases, including tumors. This has become possible thanks to a discovery made by Soviet scientists. Below is the story told by Andrei Malenkov, doctor of biology.

Though in the economically developed countries life expectancy has almost doubled in the past century, it began to show a downward trend in some countries in the 1970s. Unfortunately, the use of the most modern medicines does not lead to a substantial extension of life. What is the explanation for this situation which at first glance might seem paradoxical?

Soviet scientists L. Gavrilov and N. Gavrilova have analyzed a multitude of so-called "death-rate tables" and have concluded that in the past hundred years the aging rate has retained its regional and sex features, provided, of course, deaths from injuries, infectious diseases, and the like are not taken into account. It has been possible to extend life expectancy not by lowering the old-age death rate. We are aging at the same rate as, say, people did a hundred years ago. But science has today reached the line beyond which it will be possible to solve the problem of extending man's active life by retarding the process of aging.

There are scientists, though, who doubt this. They produce a great variety of arguments of evolutionary and social nature. But we shall proceed from the natural desire of any normal man to live longer and to remain young and full of energy for as long as possible.

Increase the Reliability of the Most Unreliable Organ

Scientists have worked out an approach to the solution of this most important problem—the so-called reliability approach, that has long and effectively been used in technology. This approach makes it possible to assess qualitatively the probability of a breakdown and to predict the time when complex mechanisms and units will fail.

For the past 10 years seminars have been held in the Soviet Union studying the question of applying the theory of reliability to biological systems. D. Grodzinsky, corresponding member of the Academy of Sciences of the Ukraine, and Y. Kutlakhmedov, D. Sc. (Physics and Mathematics) were the sponsors of these seminars in which biologists of the most diverse fields, mathematicians, physicists, and medical workers have taken part. Using the principles and the mathematical apparatus of the theory of reliability, L. Yaguzhinsky, D. Sc. (Chemistry), and L. Gavrilov, C. Sc. (Biology) of Moscow University, for example, were able to explain the main quantitative laws regulating the dependence of death probability on human age.

In technical devices the repair of a broken part can prolong the service life of the entire machine. But it is impossible to copy this experience and transfer it to the human body, because in our "machine"—in the human organism—all its components (organs) are much more closely linked with each other. And if, say, one component gets out of order, the others try to make up for its faulty work and take over its functions. The appearance of diseases depends largely on the organism's resistance to unfavorable factors. If the predisposition is passed on to the next generation, then, as it was formerly believed, it is incorporated in the organism as soon as its starts to exist, and then nothing can be changed. But it turns out that the genetic program can be "adjusted," thereby increasing the reliability of the most unreliable organ especially with respect to the processes that might lead to its failure. In other words, it is necessary to prevent chronic diseases occurring later on in life, say, when they are still in a latent state and do not make themselves felt as yet. It is necessary to raise the resistance of the organs and tissues which are most vulnerable in a given person ever since his early childhood.

Contaktin to Change the "Trajectory" of the Development of an Organ

A phenomenon discovered by Soviet biologists E. Modyanova, O. Bocharova and the author of this article has made it possible to map out an effective way of preventing chronic diseases. It has been registered in the USSR as scientific discovery No 330.

It is known that many people have a genetic predisposition to some chronic diseases, including tumors. It has also been established that tumors develop only in certain organs. People inherit not the probability of developing tumors, in general, but of tumors of some definite organ.

Geneticists have bred a great number of mice "varieties" that sharply differ in the probability of developing tumors in certain organs. Studying the force of tissue linkage in many mice "breeds" (strains), we have discovered the following fact: tumors appear only in rodents in which cell linkage in a given organ is below the level typical of that organ.

We have also established earlier that, as the tumor becomes malignant, the mechanical characteristics of its cells sharply differ from the healthy, normal tissue cells. These differences can be discovered long before the tumor appears. Biologist O. Bocharova has discovered also the last stage of the preparation of the tissue and the organ for tumor degeneration. Tumors, which are known not to develop in healthy tissues, are generally preceded by a lengthy inflammation. And if this is so, it would be

right to ask: could cell linkage be increased and, ultimately, also the tissue resistance to the development of tumors boosted? It turned out that this could be done.

By that time we had already obtained natural substances from the tissues of organs of healthy animals that were capable of restoring the strength of cell linkage. These substances were obtained in pure form by V. Yamskova, C. Sc. (Biology) at the Institute of Development Biology of the Academy of Sciences of the USSR. They were called contaktins. It has been established that it was enough to administer one-billionth of a milligram of contaktin to an animal to increase cell linkage in a given organ. Contaktin has another important property: while increasing cellular linkage, it simultaneously prevents their division (and this is the process that accompanies the growth of tumors). Unfortunately, when contaktin was injected in adult animals, these properties lasted for no more than 24 hours and then disappeared.

"And what if we gave contaktins to a young, growing organism," we thought. "Wouldn't their properties in that case last longer?"

It is known, for example, that rickets caused by vitamin D insufficiency leads to bone deformation. If you give vitamin D to an adult, it would not be of any use to him. But giving the vitamin to a child during the period of the skeleton formation would be a different matter. Then it would be possible to prevent the deformation of bones. And what if contaktin can change the "trajectory" of the development of an organ, we wondered.

We carried out a series of experiments. By administering contaktin at a critical period of development we were able to increase cell linkage in weakened organs for a rather lengthy time, and in most animals, even for the rest of their lives, and the result was that tumor incidence was reduced by 60 or 67 percent. In this way we managed to decrease the possibility of chronic pathology appearing in genetically predisposed animals.

Can our discovery be of any use for the development of medicine? Yes, it can. By using that method we will evidently be able to free people from an inherited predisposition to diseases or, at any rate, considerably reduce it, thereby helping to increase life expectancy.

/09599

Production of New Generation Electrostimulator

18400312 Moscow TASS in Russian 0520 GMT 5 Apr 88

[Summary with Excerpt] (Kiev)—"The serial production of a new-generation electrostimulator has begun in Donetsk in the Donbass of the Ukraine. It is based on a model created by Soviet scientists of a neural impulse, which allows the human muscles, tissue and organs to be acted on, provoking healing reactions."

It is known that sometimes contact with an electric current produces excellent healing results and allows medications to be kept to a minimum or even dispensed with altogether.

These new electrostimulators are very compact and so easy to use that a patient can operate them without medical supervision. The benefit is significant in cases of disorders of the neuromuscular, skeletomuscular, cardiovascular, respiratory, and digestive systems, and metabolic disorders. Tests in the country's major clinics bear this out.

The new instruments are also indispensable in maintaining the work capacity of a healthy person and in reducing fatigue and will be widely used in workplaces where there is limited scope for movement—assembly lines, road and rail transport and civil aviation.

/09599

Effect of a Mixture of Synthetic Sugars on Growth and Luminescence of Bacteria

18400246 Moscow MIKROBIOLOGIYA in Russian Vol 56, No 5, Sep-Oct 87 (manuscript received 21 Mar 86) pp 774-777

[Article by I. P. Dzhunkovskaya and V. I. Sukharevich, Leningrad Technological Institute imeni Lensovet]

[Abstract] Growth and luminescence of light-producing bacteria depends on the cultivation conditions. The goal of this work was to investigate the effect of a mixture of synthetic carbohydrates—formose—on the growth and bioluminescence of P. fischeri bacteria. At concentrations of 1 x 10^{-4} to 1 x 10^{-2} mass percent, formose stimulated biomass synthesis. Bacterial luminescence intensity approximately paralled the increase in the biomass. The yield of luciferase did not change, hence formose appeared to be affecting only culture growth. At higher concentrations of formose, growth and luminescence were inhibited due to catabolic repression of luciferase synthesis. In the presence of cyclic AMP this latter effect was eliminated. Luminescence was repressed by the principal components of formose: glucose and xylose. Cyclic AMP eliminated the effect of xylose but not that of glucose. Figures 3; references 12: 4 Russian, 8 Western.

7813/9604

Nuclear Magnetic Resonance Study of Ricin Conformation. High Mobility of N-Terminal Sections of A and B Subunits

18400199a Moscow MOLEKULYARNAYA BIOLOGIYA in Russian Vol 21, No 6, Nov-Dec 87 (manuscript received 17 Dec 86, revised manuscript received 23 Mar 87) pp 1686-1693

[Article by A. G. Tonevitskiy and V. N. Bushuyev, All-Union Cardiological Scientific Center, USSR Academy of Medical Sciences, Moscow]

[Abstract] Ricin was obtained from castor bean plant seeds (Ricinus communis) by the Nicolson and Blaustein method and A- and B-chains were isolated by the Olenes and Phil method. Analysis of ^{1}H-NMR spectra (500 MHz) of ricin and its isolated A- and B-subunits showed that there are flexible, highly mobile segments together with close packing of the polypeptide chain in the structure of the proteins. Spin-echo sequence (90° τ-180° τ) was used to suppress forbidden wide signals from amino acid residues in the globular structure and to isolate selectively narrow signals from highly mobile side chains. Study of the narrow signals and analysis of the width of the lines showed that N-terminal sections of the polypeptide chains of A- and B-subunits are free and have high segmental mobility. Figures 5; references 21: 1 Russian; 20 Western.

02791

Effect of Gangliosides Gm1 and Gm3 on Binding, Internalization and Cytotoxic Activity of Ricin

18400199b Moscow MOLEKULYARNAYA BIOLOGIYA in Russian Vol 21, No 6, Nov-Dec 87 (manuscript received 13 Feb 87) pp 1694-1701

[Article by A. G. Tonevitskiy, O. S. Zhukova, N. V. Timofeyeva and L. D. Bergelson, All-Union Cardiological Scientific Center, USSR Academy of Medical Sciences, Moscow; Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow]

[Abstract] Treatment of Burkitt lymphoma EB-3 cells with gangliosides Gm1 and Gm3 caused their binding and partial incorporation into the plasma membrane. About 25 percent of ganglioside Gm1 bound with the cells could interact with the B-subunit of ricin and this produced a 3-fold increase of binding of the toxin by cells treated with 0.2 mM ganglioside Gm1. Increase of the number of ricin binding sites upon incorporation of ganglioside Gm1 into the cell decreased the cytotoxic activity of ricin rather than increasing it. Treatment with ganglioside Gm3 produced a similar effect. A 20-fold increase of binding sites after treament of cells by neuraminidase produced a 6-fold increase of ricin cytotoxic action. The rate of disappearance of ricin from the surface of intact cells and cells treated by ganglioside was assessed by use of antibodies to the B-chain of ricin. A 20-minute incubation at 37°C resulted in about 15 percent of bound ricin on the surface of intact cells and 35 percent on that of cells treated with ganglioside Gm1. About 10 percent of the toxin remained after 60 minutes. The differences seen in the rate of endocytosis was attributed to differences in cytotoxic activty of ricin in relation to intact cells and to lymphoma cells treated with ganglioside. It was assumed that only high-affinity receptors, making up 1 percent of all binding sites, are responsible for the cytotoxic effect of ricin. Figures 5; references 22: 3 Russian; 19 Western.

02791

P-Element Transfer into Drosophila hydei Embryonic Cells and Mouse Bone Marrow Cells

18400215 Yerevan DOKLADY AKADEMII NAUK ARMYANSKOY SSR in Russian Vol 85, No 4, 1987 pp 172-176

[Article by R. A. Zakharyan and S. G. Bagrazyan, Institute of Experimental Biology, Armenian SSR Academy of Sciences]

[Abstract] Gene transfer into the cells of higher eukaryotes by introduction of allogenic genetic information involves integration of the introduced gene into the genome, its expression and the stably inherited and preserved change in the phenotype of recipient cells. The use of transposon-like genes of eukaryotes in order to increase the frequency of transformation and integration of the introduced gene into a specific site in the genome is of interest. This article describes a study of the possibility of transposition from a recombinant plasmid and functioning of the P-element in embryonic cells of Drosophila hydei, which is related to Drosophila melanogaster, and in mouse bone marrow cells. The Dr. hydei genome did not contain sequences homologous to the P-element gene. However, in myeloid cells of mice, the P-element has the capacity for autonomous replication and replicative transposition of the intact gene within the genome of mouse myeloid cells. Figures 3.

02791

Transformation of Eukaryotic Cells by DNA in Reconstructed Nucleoprotein Complexes

18400236a Kiev BIOPOLIMERY I KLETKA in Russian Vol 4, No 1, Jan-Feb 88 (manuscript received 21 Jan 86) pp 48-53

[Article by R. A. Zakharyan, G. G. Galstyan, N. R. Gevorkyan, M. G. Galstyan and L. M. Amirkhanova, Institute of Experimental Biology, Armenian SSR Academy of Sciences, Yerevan]

[Abstract] An attempt was made to use anionic DNA-binding plasma proteins as a self-assembly factor of nucleosome-like structures and to study the effectiveness of gene transfer from reconstructed nucleosome-like structures into mammalian cells. It was shown that acidic DNA-binding plasma proteins facilitated the

reconstruction of nucleosome-like complexes from histones and purified DNA at low ionic strength. The smallest size of the DNA fragments in these structures was 140 base pairs. These nucleosome-like complexes exhibited biological activity in transforming eukaryotic (Ltk^-aprt^-) cells. The transforming activity of DNA in these complexes was of an order of magnitude higher than that of the DNA in the Ca^{2+}-precipitate. Thus the potential of using acidic DNA-binding plasma proteins in reconstruction of nucleosome-like structures on the basis of individual genes was demonstrated along with transformation of mammalian cells by these complexes. Figures 2; references 27: 1 Russian, 26 Western.

7813/9604

Status of T- and B-Components of the Immune System Shortly After Local Exposure to Microwaves

18400204b Frunze ZDRAVOOKHRANENIYE KIRGIZII in Russian No 6, Nov-Dec 87 pp 30-33

[Article by V. M. Yevstropov, I. N. Silich, R. A. Zulkarneyev, O. P. Modnikov and N. G. Lomtev, Kirgiz Scientific Research Institute of Health Resort Science and Physical Therapy; Kirgiz Scientific Research Institute of Oncology and Radiology]

[Abstract] The authors studied the response of the T- and B-components of the immune system to irradiation of the central organs of the immune system, the thymus and bone marrow, with decimeter electromagnetic waves. Experiments were performed on 261 guinea pigs. Decimeter waves bombarded the thymus (ventral surface of the neck) and bone marrow (tibia) by means of a 4 cm diameter contact radiator operating at 80 mW/cm^2. A single ten minute session of irradiation of the thymus did not influence the content of T- and B-lymphocytes in the blood, although five daily ten minute sessions decreased the number of T-lymphocytes. One-time irradiation of the bone marrow decreased the number of T- and B-cells, while five irradiation sessions increased the level of O-lymphocytes. The functional activity of the T-system was unchanged after the first session, but decreased after the fifth session of thymus irradiation. The functional activity of the B-system also changed after the fifth session, increasing regardless of the location of radiation. Decimeter radiation applied to the thymus and bone marrow thus caused different changes in the structural and functional status of the T- and B-components of the immune system soon after irradiation. This probably results from the relative specialization of the lymphoid organs studied, the thymus being primarily related to the T-system, the bone marrow — to the B-system.

06508

Manufacture of Proserine Tablets Containing High-Molecular Additives and Study of Their Properties

18400207 Moscow FARMATSIYA in Russian No 6, Nov-Dec 87 (manuscript received 29 Dec 86) pp 22-23

[Article by T. N. Zakrzhevskaya and G. I. Lukyanchikova, Pyatigorsk Pharmaceutical Institute]

[Text] In modern medicine, proserine has found wide application as an anticholinesterase drug. But its action is not prolonged [4]. In previously conducted research we established the possibility of prolonging the effect of medicinal compounds using binding substances [2].

The goal of this work is to study the possibility of prolonging the effect of proserine tablets using the auxiliary binding substances gelatin, methylcellulose (MC), and polyvinyl alcohol (PVA), which are high-molecular-weight compounds (HMC).

Experimental Section

Preliminary studies established that the concentration of aqueous solutions of the HMCs should not exceed 10 to 15 percent, taking into account their solubility in water.

In order to study the granulating capacity of HMC solutions, granulation was carried out according to the general procedure in [5]. The conditions of granulation were: drying temperature of granules of 30°C, drying time of 2-3 hours, residual moisture of 1.8-2.0 percent. The quality of the granules obtained, determined according to their fractional composition, is shown in Table 1.

TABLE 1. Fractional Composition of the Granulate with Various Binding Substances

Binding Substance	Concentration of the Binder Solution, %	Size of Particles, mm		
		Up to 0.25	0.25-0.5	Greater than 0.5
Gelatin	5	42.7	28.5	28.8
	10	36.3	38.1	25.6
	15	35.4	42.3	22.3
MC	5	27.9	34.1	38.0
	10	22.4	46.8	30.8
	15	25.8	44.7	29.5
PVA	5	25.2	41.3	33.5
	10	20.8	45.0	34.2

From Table 1 it is clear that when MC and PVA solutions are used, the granulate is more uniform than when the gelatin solution is used, when the amount of the small fraction predominates.

For moistening, various quantities of the binder solutions were added in proportion to the mass of the granules. Research has proven that in using MC and PVA, the necessary properties of the mass are secured by using binder solutions added in the amount of 3 percent of the total mass of the granules.

Based on the known properties of friability agents recommended by GFKh [State Pharmaceutical Industry] [1], the effect of the presence of talc and of a 1:1 mixture of talc and starch on the granules was studied. It was established that the granules possess the necessary technological properties of friability both with talc and with the mixture of talc and starch. The 1:1 mixture of talc and starch turned out to be preferable; its use reduced the concentration of talc in the composition of the granules. The necessary content of friability agents was determined by comparing the mass of granules.

It was experimentally established that the optimal quantity of friability agents is 2 percent. When the concentration is increased, the properties of the granulated mass are almost unchanged.

In experimental pressing of the granulated mass, the tablets adhered to the die. In order to eliminate this defect, the addition of stearic acid in the amount of 1 percent of the total mass of the granules turned out to be useful.

Based on the research carried out, we propose for further study the following recipe for model tablets:

Proserine	0.015 g
Sugar	0.276 g
Talc and starch, 1:1	0.006 g
Stearic acid	0.003g
MC or PVA, 5 or 10% solution	0.009 g

Tablet formation was carried out at a constant operating pressure of molding. The tablets produced met the requirements of GFKh [1]. Taking into account the effect of high-molecular compounds on the release of drugs from medicinal forms, the dynamics of the release of proserine from the tablets was studied [6]. This study was carried out by dialysis through cellophane. Observations were taken after each hour, selecting samples of the dialysate, in which the concentration of proserine was determined.

TABLE 2. Dynamics of Proserine Release from Tablets

Duration of Dialysis, Hours	Concentration of Proserine in the Dialysate, %			
	Solutions of MC		Solutions of PVA	
	5	10	5	10
1	23.0+-0.55	26.5+-0.60	29.6+-0.68	30.0+-0.73
2	31.8+-0.76	35.4+-0.81	30.0+-0.72	32.0+-0.73
3	35.8+-0.81	37.6+-0.92	35.0+-0.83	35.2+-0.82
4	43.3+-0.92	43.6+-0.93	35.5+-0.83	35.9+-0.81
6	43.3+-0.90	42.1+-0.88	35.9+-0.84	36.3+-0.88
12	61.9+-1.46	58.9+-1.38	51.6+-1.33	50.5+-1.30

In order to quantitatively assess the release of proserine, we used a previously worked out methodology of extraction-photometric determination of proserine, based on reactions forming ionic associates with bromothymol blue (BTB) [3].

The following items were introduced one by one into a separating funnel: 8 ml citrate-alkali buffer solution with pH 6.4; 0.8 ml dialysate, 1.2 ml of a 0.1 BTB solution, and 5 ml chloroform. The contents of the funnel were stirred over the course of 2 minutes and then the chloroform layer was separated off. The optical density of the extract was measured using a photoelectrocolorimeter in a 5 mm cell at a wavelength of approximately 434 nm. A chloroform extract of BTB at pH 6.4 was used as the comparison solution.

The proserine concentration (in percent) was determined by comparison with a 0.01 percent standard solution of proserine which was introduced into the separation funnel in the amount of 0.8-0.9 ml.

The release of proserine as a function of the nature and concentration of solutions of auxiliary binders is shown in Table 2.

From Table 2 it is clear that PVA added to the tablets secures a more constant rate of proserine release than MC. PVA slows the release of proserine by 6-10 percent, which helps to create and maintain a greater prolonging effect.

Conclusions

1. The technology of manufacturing proserine tablets containing methylcellulose and polyvinyl alcohol was thoroughly studied.

2. The use of polyvinyl alcohol substantially influences the release of proserine from tablets and, consequently, causes a prolonging effect.

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12255

Effect of 1-(Chloromethyl) Silatrane on Blood Element Alteration During Cardiopulmonary Bypass

18400195a Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 10, Oct 87 (manuscript received 12 Jan 87) pp 418-420

[Article by Yu. B. Pisarskiy, V. B. Kazimirovskaya and M. G. Voronkov, Irkutsk Institute of Organic Chemistry, USSR Academy of Sciences, Siberian Department]

[Abstract] Use of an artificial blood circulation apparatus during heart surgery, use of auxiliary blood circulation to treat cardiac insufficiency and prostheses of heart valves and main arteries sometimes traumatize blood

elements. It has been shown that 1-(chloromethyl)silatrane (CMS) protects blood element membranes during their alteration by ultrasound and as a result of perfusion. Therefore, this study investigated the prospects of using CMS as a blood element protector during extracorporeal blood circulation. CMS was injected intravenously into dogs (1 mg/kg dose) in 10 ml of physiological solution and the dogs were subjected to extracorporeal blood circulation for 3 hours. The effect on the integrity and functional activity of blood elements was determined by the hemoglobin level in blood plasma, kinetics of lipid peroxidation in blood serum as measured by a chemoluminescence method and erythrocyte resistance to ultrasound. CMS doses used in the study produced a significant protective effect during the extracorporeal blood circulation. It reduced the rate of entry of Hb into the blood plasma, increased membrane resistance to ultrasound and kept the erythrocyte membrane resistance to ultrasound at the initial level throughout the experiment. CMS reduced activation of lipid peroxidation action in the first 15 minutes and kept it at the initial level for some time. A possible mechanism of the damaging effect on blood elements during cardiopulmonary bypass was discussed. Stabilization of the structure and function of blood elements was attributed to the capacity of CMS to regulate the intensity of lipid peroxidation in the biological membranes. Figures 3; references 14: 13 Russian; 1 Western.

02791

Effect of Bemithyl on Perception of Visual Stimuli

18400195b Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 10, Oct 87 (manuscript received 20 Feb 87) pp 455-456

[Article by Yu. G. Bobkov, A. I. Machula and E. G. Dvalishvili, Scientific Research Institute of Pharmacology, USSR Academy of Medical Sciences; All-Union Scientific Research Center on Biomedical Problems of Intoxication and Alcoholism Prevention]

[Abstract] An analysis of the effect of bemithyl on purposeful behavior included the study of 3-3.5 kg cats trained by the method of conditioned-defensive reflexes to discriminate two differently oriented lines presented with different times of exposure ranging from 300-5000 ms. Training was assumed to be complete if the cats differentiated stimuli of 3000 ms duration in almost 100 percent of the cases. Differentiation of short stimuli [DKS] (500 ms), differentiation of long stimuli [DDS] (3000 ms), latent period of conditioned reflex to differentiated stimuli [LPD] and to a single stimulus [LPO], time required to make a decision [VPR] and number of inter-stimulus reactions [MR] were determined upon presentation of visual stimuli to the cats (3-3.5 kg) after intravenous injection of bemithyl (15 mg/kg or 30 mg/kg). Proper identification of visual stimuli, presented for 3000 ms, occurred in 90-95 percent of the cases after 25-30 training sessions. A 15 mg/kg dose of bemithyl did not change DKS nor DDS; decreased LPD and LPS and did not change VPR nor the number of MR. A 30 mg/kg dose improved DKS, did not change DDS, increased the rate of reaction to LPD and LPO stimuli, did not change BPR but decreased the number of MR. A 30 mg/kg dose reduces the anxiety level. References 6 (Russian).

02791

Analysis of Functional State of Brain Under Effect of Bemithyl, Using Theoretical Methods of Image Recognition

18400196b Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 11, Nov 87 (manuscript received 20 Feb 87) pp 574-576

[Article by Yu. G. Bobkov, A. N. Machula, Yu. I. Morozov and E. G. Dvalishvili, Scientific Research Institute of Pharmacology, USSR Academy of Medical Sciences; All-Union Scientific Research Center on Biomedical Problems of Intoxication and Alcoholism Prevention, Moscow]

[Abstract] Behavioral and electrophysiological indicators were recorded for further analysis of the effect of bemithyl on central nervous system activity. Electrodes, implanted in cats trained to react differentially to structured visual stimuli, recorded evoked potentials of the visual, parietal associative and secondary somatosensory zones of the neocortex in response to the conditioned stimuli presented. Bioelectrical activity was recorded on a special PARK-42-02 computer after intraperitoneal injection of bemithyl (30 mg/kg) and data obtained were processed on a general purpose computer. Behavioral parameters recorded include differentiation of short and long visual stimuli, latent period of reaction to differentiated and single stimuli, time of reception and number of interstimuli reactions. The method of cluster analysis was emphasized. Bemithyl increased the degree of association between all functional elements of the system. It reduced the importance of the process of entry of information into the visual region of the neocortex and decreased the importance of activity of the associative region. The effect of bemithyl on the structure of the physical model of the visual stimulus was not due to its direct effect on the sensory structures but is mediated by the effect on other processes which, in turn, produce a constant correcting effect on analysis of physical properties of the external world. The state arising after bemithyl injection differed greatly from the background state, indicating the realization of the behavorial reaction by other than the background pathways and has been attributed to the early effect of bemithyl on nervous tissue energetics. References 8: 7 Russian; 1 Western.

02791

Combined Pathogenetic Therapy of Experimental Botulinum Intoxication

18400196a Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 11, Nov 87 (manuscript received 18 Dec 86) pp 543-545

[Article by G. N. Kryzhanovskiy and V. V. Morrison, Laboratory of General Pathology of the Nervous System (headed by Academician of USSR Academy of Medical Sciences, Professor G. N. Kryzhanovskiy), Institute of General Pathology and Pathological Physiology, USSR Academy of Medical Sciences, Moscow; Department of Pathological Physiology (headed by Professor N. P. Chesnokova), Saratov Medical Institute]

[Abstract] Male white mice (20-22 g) and white rats (200-220 g) received botulinum toxin type C intramuscularly in the rear extremity (0.2, 0.16 or 0.14 μg/mouse and 10 μg/rat), and the survival rate and length of survival of the animals revealed the effectiveness of 4-aminopyridine (1 or 2 mg/kg) intraperitoneally twice a day and gutimine injected intraperitoneally (50, 100 or 200 mg/kg). Drugs were administered immediately after botulinum toxin injection. Combined use of the drugs produced excitation and increased motor activity in the animals within 10-15 minutes after injection. Combined use of the drugs produced a more pronounced protective effect than did use of the drugs separately. Relatively small doses of the drugs in combination produced the greatest protective effect. Combined use also caused a significant increase of the mean lethal doses of the toxin. The potentiation effect of the drugs when used in combination made it possible to reduce the dosage and reduce the probability or the degree of side effects. Thus, the combined therapy promoted transmitter release and provided protection against experimental botulinum intoxication and may be a useful addition to existing methods of treatment of botulism. Figures 2; references 16: 13 Russian; 3 Western.

02791

Behavioral and Electrophysiological Characteristics of L-Pyroglutamyl-D-Alanine Amide, Peptide Analog of Piracetam

18400196c Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 11, Nov 87 (manuscript received 2 Mar 87) pp 576-579

[Article by R. U. Ostrovskaya, T. A. Gudasheva, S. S. Trofimov, G. A. Romanova, V. P. Dobrynin, N. F. Sepetov, O. L. Isakova and A. P. Skoldinov, Scientific Research Institute of Pharmacology, USSR Academy of Medical Sciences; Scientific Research Institute of General Pathology and Pathological Physiology, USSR Academy of Medical Sciences; Scientific Research Institute of Experimental Cardiology, All-Union Cardiological Research Center, USSR Academy of Medical Sciences, Moscow]

[Abstract] The stability of L-pyroglutamyl-D-alanine amide, its effect on trainability of rats and an electrophysiological analysis of its effect on the integrative function of the brain were described and discussed. The stability of the compound was studied in vitro at 37°C by H-NMR spectroscopy. The effect of the compound on trainability of rats was assessed by its effect on conditioned reflexes of active and passive avoidance. The compound was very stable in the presence of blood serum enzymes. A 1 mg/kg dose of the compound intraperitoneally (as compared to 200 mg/kg of piracetam) increased trainability of the rats and facilitated all phases of processing of the memory engram. The compound is selective (as is piracetam) and did not produce concomitant psychomotor excitation. The study showed the compound to be a stable peptide analog of piracetam but having a wider spectrum of effect and higher activity. Figures 2; references 13: 10 Russian; 3 Western.

02791

Role of GABA-ergic System in Mechanism of Stress-regulating Effect of Phenibut

18400196d Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 11, Nov 87 (manuscript received 17 Jun 86) 588-590

[Article by G. V. Kovalev, A. A. Spasov, N. A. Bogachev, V. D. Petryanik and O. V. Ostrovskiy, Department of Pharmacology (headed by Professor G. V. Kovalev) and Central Scientific Research Laboratory (director—senior scientist S. A. Nikitin), Volgograd Medical Institute]

[Abstract] The effect of phenibut on activity of the γ-aminobutyric acid [GABA] system under normal conditions and during stress was studied in experiments with 75 male white mongrel rats (weight 120-170g) with determination of the GABA level, glutamic acid level and activity of GABA metabolism enzymes in the hypothalamus and thalamus. The degree of pronouncement of the stress reaction was determined by the P-hydroxycorticosteroid and glucose levels in peripheral blood plasma. Rats were deprived of food and water and suspended by a neck skin fold and then decapitated after 3, 18 or 48 hours of stress. Phenibut was injected subcutaneously in a single optimum stress-regulating dose of 1 mg/kg 45-60 minutes before the 3 and 18-hour stress period and was injected a second time after 24 hours in the 48-hour period of stress. Phenibut had practically no effect on the GABA and glutamic acid level in the thalamus and hypothalamus and did not change the P-hydroxycorticosteroid or glucose level in the peripheral blood. Phenibut increased glutamate decarboxylase activity 1.6-fold and GABA-transaminase activity 1.5-fold within 1 hour after injection. The effectiveness of GABA as a neuromediator in emergency adaptation of the body was significant only during short-term stress. Preliminary activation of the GABA-shunt increased the resistance of the GABA system as a whole and increased the duration of its functioning during adaptation of the body to extreme conditions. Figures 2; references 16: 12 Russian; 4 Western.

02791

Dynamics of Certain Functional Changes in the Kidneys Upon Exposure to Cobra Venom

18400203 Ashkhabad ZDRAVOOKHRANENIYE TURKMENISTANA in Russian No 8, Aug 87 pp 21-24

[Article by A. T. Berdyeva, B. B. Batyrov and L. A. Molotova, Department of Biology (headed by Professor A. T. Berdyeva), Turkmen Order of International Friendship State Medical Institute (Rector—Professor N. N. Nurmamedov); Scientific Research Institute for Protection of the Health of Mothers and Children (Directed by Doctor of Medical Sciences V. Ye. Radzinskiy), Turkmen SSR Ministry of Health]

[Abstract] The purpose of this work was to study some of the partial functions of the kidneys (diuresis, glomerular filtration, tubule reabsorption) during the course of poisoning with various doses of cobra venom under experimental conditions. Experiments were performed on 244 white rats of both sexes in special metabolic cages, in which urine was collected each hour for four hours after administration of a solution of cobra venom or saline solution in the control animals. Four doses were used: 1.1, 1.3, 1.5 and 1 LD_{50}. The animals were sacrificed 1, 2, 3 or 4 hours after administration of the venom. The content of endogenous creatinin was determined in urine and blood plasma, urine volume was measured, and the level of glomerular filtration and tubule reabsorption determined. The results indicated that the toxic effect of the cobra venom was directed at the glomerular infiltrate and the capability of the tubules for reabsorption, causing the development of acute renal insufficiency. Small doses of the poison, causing no visible clinical symptoms, increased diuresis and at the same time increased the content of creatinin in urine. References 16: 10 Russian, 6 Western.

06508
UDC 615.356:577.161.3].012.1.07

Synthesis, Properties, and Detoxifying Activities of Analogs and Derivatives of Alpha-Tocopherol

18400229 Moscow KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Vol 21, No 12, Dec 87 (manuscript received 3 Dec 86) pp 1441-1446

[Article by V.P. Makovetskiy, V.D. Lukyanchuk, and V.I. Kalinina, Institute of Organic Chemistry, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] The demonstration that α-tocopherol is one of the more effective detoxifying agents led to the present study to assess a series of previously synthesized analogs and derivatives of α-tocopherol for similar physiological efficacy. The studies were conducted with 160-210 g male and female outbred rats treated twice at one day intervals per os with the sodium salt of dinitro-ortho-cresol (35 mg/kg). The agent to be tested was administered intramuscularly (30 mg/kg) 3 or 24 h before the administration of the cresol. The survival and toxicity studies demonstrated that virtually all of the preparations tested rendered some degree of protection. Compounds with a shortened chain at position 2 and concomitant addition of an unsaturated bond in the chain enhance protective activity compared to α-tocopherol. However, complete elimination of the side chain with disruption of the dihydrobenzopyran ring and formation of p-quinoid structures has no essential effect on activity. Introduction of a furan system was not beneficial, but benzofurans improved both the survival figures and attenuated toxic manifestations of the cresol compound. The phenol analogs showed variable effects depending on a number of structural factors. In general, however, the simpler analogs of α-tocopherol potentiated the detoxifying activity against dinitro-ortho-cresol. References 17: 13 Russian, 4 Western.

12172/06662

UDC 615.214.015.4:612.821.058:591.555

Computerized Ethopharmacology

18400226a Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 50, No 6, Nov-Dec 87 (manuscript received 28 Apr 87) pp 5-13

[Article by V. P. Poshivalov, Department of Pharmacology, Central Scientific Research Laboratory, First Moscow Medical Institute imeni I. P. Pavlov, Leningrad]

[Abstract] A review is presented of current developments in ethopharmacology as a special aspect of experimental psychopharmacology. In the USSR, additionally, the field is distinguished by the fact that emphasis is being placed on computerized data processing as part of a systemic approach to the problem. Various mathematical models, both discrete and continuous, are being developed for data handling and interpretation. For example, advances in discrete modeling have relied on the APPROX program for Lagrange algorithms for discontinuous polynominal approximations of behavior patterns. With the development of the field of endogenous opioids, additional parameters have been introduced into purely pharmacological studies, with the development of hypothetical control mechanisms for aggressiveness, avoidance, and normal social behavior involving this class of endogenous peptides and neurotransmitters. Future advances in ethopharmacology will depend on standardization of research methods as well as improved classification and definition of psychotropic agents. Figures 1; references 34: 9 Russian, 25 Western.

12172/9274

UDC 615.214.3:547.754].076.9

Functional and Morphological Characteristics of Stress-Protective Action of Piracetam

18400226b Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 50, No 6, Nov-Dec 87 (manuscript received 12 Jun 86) pp 14-16

[Article by V. M. Vinogradov, A. A. Klishov, V. F. Katkov, A. V. Smirnov, Ye. B. Katkova, V. G. Gololobov, G. Ya. Grafova, Yu. N. Khilova and V. N. Vinogradova, Leningrad]

[Abstract] The demonstration that piracetam has a positive effect on higher nervous function in various stressful conditions led to a further evaluation of its effects in animals subjected to conditions evoking the stress syndrome. The study was conducted with 150-200 g male rats deprived of food, water, and sleep for two days on a slowly rotating drum. Experimental animals were treated intraperitoneally with 50 mg/kg piracetam b.i.d., with subsequent analysis of their behavior patterns, physical fitness, and histopathological changes in various organs. The untreated control animals demonstrated physical debility and deterioration of the functional capacity of the higher nervous system, as well as extensive histological lesions in the brain, heart, liver, and thymus. Piracetam-treated rats demonstrated greater tolerance of physiological stress, diminished ulceration of gastric mucosa, and attentuation of thymic involution or atrophy in comparison with the untreated rats. Most importantly, treatment of the experimental rats with piracetam resulted in retention of normal brain histology without the type of hyperchromatosis evident in the untreated animals. Tables 1; references 5 (Russian).

12172/9274

UDC 615.214.31.015. 4.076.9

Comparative Neurophysiological Studies on Nootropic Agents Piracetam and Centrophenoxine

18400226c Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 50, No 6, Nov-Dec 87 (manuscript received 11 Feb 86) pp 17-20

[Article by S. V. Krapivin and T. A. Voronina, Institute of Pharmacology, USSR Academy of Medical Sciences, Moscow]

[Abstract] A comparative neuroelectrophysiological study was conducted on piracetam and centrophenoxine, two established nootropic agents, to determine whether similar mechanisms of action were responsible for their neuropsychological effects. The effects of both agents on transcallosal evoked potentials (TEP) were assessed in rabbits free of anesthetics or myorelaxants, while the effects of cortical and hippocampal EEG spectra were evaluated in unrestrained rats. Both agents led to an increase in the first positive component (P_1) and the first negative component (N_1) of TEP by ca. 50 percent or more. However, while piracetam also increased the amplitude of the second positive component (P_2), centrophenoxine administration led to its depression. Thus, the administration of 25-200 mg/kg intraperitoneally of either agent appeared to facilitate conduction between the cerebral hemispheres. However, the mechanisms responsible for this phenomenon were different in the case of piracetam and centrophenoxine as indicated by their effects on P_2. Studies on rabbits demonstrated that piracetam stabilized and enhanced the dominant peak (6-7 Hz) in the theta band of the EEG within 1-1.5h of administration by ca. 30 percent in the cortex, and by 68 percent in the hippocampal EEG. Centrophenoxine showed stabilization and ca. 77.5 percent enhancement in the cortex within 0.5-1.0 h, and in the hippocampus within 0.5-1.5 h by ca. 83 percent. Furthermore, centrophenoxine also enhanced the 2nd peak (10-12 Hz) within 0.5 h, an effect not seen with piracetam. These observations indicate that piracetam and centrophenoxine exert their nootropic effects by means of different mechanisms, which are presumably cholinergic in the case of the latter agent. Figures 3; references 9: 4 Russian, 5 Western.

12172/9274

UDC 615.31:[547.95:547.943].076.9

Evaluation of Analgesic Properties of Nucleoamino Acid Analogs of Neuropeptides on Intracisternal and Intravenous Administration to Mice

18400226d Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 50, No 6, Nov-Dec 87 (manuscript received 18 Jun 86) pp 20-23

[Article by O. N. Ryabtseva, M. G. Petrova, G. A. Korshunova, O. N. Chichenkov and Yu. P. Shvachkin, Department of Pharmacology, Therapeutic and Sanitary-Hygienic Faculties, First Moscow Medical Institute imeni I. M. Sechenov; Department of Chemistry of Natural Substances, Chemical Faculty, Moscow State University imeni M. V. Lomonosov]

[Abstract] In an attempt to obtain novel analgesic agents based on endogenous peptides (opioids) that would also display enhanced half-life in the body due to their resistance to peptidases, the analgetic properties of a series of analogs of kyotorphin and enkephalin—in which certain amino acids were replaced by nucleoamino acids—were tested on 23-27 g outbred white mice. The replacement moieties consisted of L-β-(adenyl-N^9)-α-alanine, L-β-(thyminyl-N^1)-α-alanine, or L-β-(uracilyl-N^1)-α-alanine. Intracisternal injections of kyotorphin (10-200 μg) or of its analogs (20-50 μg) did not show any consistent pattern of analgesia in a tail-clip test. The kyotorphin analogs in which the tyrosine moiety was replaced by a nucleoamino acid showed some analgesic properties at near-toxic doses. Evaluation of enkephalin

and 18 of its analogs (all analogs with D-alanine or D-phenylalanine in the 2nd amino acid position) showed that the parent peptide and most of its analogs possessed analgesic activity that exceeded or equaled that of morphine on intracisternal injection. On intravenous administration these peptides were far less effective, falling significantly below the efficacy of morphine. The latter observation was attributed to limited ingress into the CNS because of the blood-brain barrier. Tabes 2; references 11: 4 Russian, 7 Western.

12172/9274

UDC 615.31:547.46].03:616.89-008.441.13].076.9

Preclinical Toxicity Trials With Novel Antialcoholic Agent Inmecarb

18400226e Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 50, No 6, Nov-Dec 87 (manuscript received 27 Mar 86) pp 80-82

[Article by B. I. Lyubimov, N. M. Smolnikova, A. N. Yavorskiy, S. N. Strekalova, S. S. Boyko, I. G. Kurochkin, L. P. Kovalenko, A. M. Krylova, A. V. Sorokina, G. R. Marakova and Ye. P. Nemova, Laboratory of Drug Toxicology, Institute of Pharmacology, USSR Academy of Medical Sciences, Moscow]

[Abstract] Animal studies have demonstrated that inmecarb (β-dimethylaminoethyl 1-benzyl-2,3-dimethylindole-5-carbonate hydrochloride), a putative antialcoholic agent, depresses ethanol intake, while preliminary clinical trials have provided similar indications, particularly in patients in early stages of alcoholism. To further expand the preclinical toxicity data base with regards to inmecarb, comprehensive toxicity evaluations were conducted on rats, guinea pigs, and dogs. The drug was administrated in various dosages (10 to 300 mg/kg in rats; 1/5 LD_{50} = 300 mg/kg) with extensive histopathological, biochemical, hematological, mutagenic, embryotropic, and allergenic monitoring. Administration of the drug on a daily basis for 6 months demonstrated that inmecarb was relatively nontoxic. There was no evidence of any allergenic potential, embryotoxicity, or of mutagenicity. Hematologic changes in the same animals were of a limited nature, as were biochemical indications of metabolic disorders. Administration of inmecarb in doses of 100 and 300 mg/kg to rats for 6 months induced an increase in the weight of the adrenal glands and a loss of thymic and splenic weight. Histological examinations showed no changes in most of the animals, with only the most reactive rats displaying slight or moderate histopathology. Overall, these observations demonstrated that inmecarb is a relatively nontoxic agent. The changes that were seen pertained only to subtoxic doses and were moderate and reversible. References 4 (Russian).

12172/9274

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Therapeutic and Prophylactic Efficacies of Zyxorin in Intoxication With Anticholinesterase Pesticides

18400226f Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 50, No 6, Nov-Dec 87 (manuscript received 21 Apr 87) pp 97-100

[Article by N. V. Kokshareva, Yu. S. Kagan, L. M. Ovsyannikova, S. Seberini and D. Ungvari, Department of Experimental Toxicology and Pathology of Chemical Etiology, All-Union Scientific Research Institute of Hygiene and Toxicology of Pesticides, Polymers, and Plastics, USSR Ministry of Health, Kiev]

[Abstract] The novel compound zyxorin (m-trifluoromethyl-α-ethylbenzhydrol) has been shown to possess the same spectrum of activity as phenobarbital in terms of offering protection against pesticides inhibiting cholinesterase, but offering the distinct advantage of being ca. 10-fold less toxic. In the present case the therapeutic and prophylactic potentials of zyxorin were studied on 180-220 g albino rats subjected to acute and subacute intoxication by a series of organophosphorus and carbamate pesticides. Intragastric administration of zyxorin (50 or 100 mg/kg) enhanced the activity of cytochrome P-450 by 238 percent in comparison with control values, and induced a 212-216 percent increase in the activities of N- and O-demethylases in hepatic microsomes. Pretreatment of the animals with zyxorin (50 mg/kg) reduced the toxicity of subsequently administered organophosphorus and carbamate compounds 1.43-1.70-fold and also enhanced the tolerance to chlorophos 1.60-1.68-fold. Electrophysiological studies also demonstrated that zyxorin overcame neuromuscular conduction block due to these pesticides. Administration of zyxorin in combination with chlorophos or pirimor (the latter in 0.5 LD_{50} doses) for 5 days prevented death and enhanced the activity of cytochrome P-450 by 172-200 percent. Either pesticide alone significantly depressed cytochrome P-450. Finally, the use of zyxorin (50 mg/kg four times) in combination with atropine and the conventional cholinesterase reactivators dipyroxime and diethyxime prior to intoxication with O,O-dimethyl-O-2,2-dichlorovinyl phosphate improved the therapeutic efficacy of the combined chemotherapy to the extent that the animals tolerated an additional 1.5 LD_{50} dose. These findings demonstrated that zyxorin is an effective prophylactic and therapeutic agent for pesticides inhibiting cholinesterase, with a mechanism of action analogous to that of phenobarbital. Figures 1; tables 2; references 8: 6 Russian, 2 Western.

12172/9274

Specific Binding of Tritium-Labeled SKF 10047 to Mouse Splenocytes

18400234c Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 12, Dec 87 (manuscript received 16 Feb 87) pp 700-703

[Article by K. N. Yarygin, G. T. Sukhikh, V. A. Vinogradov and G. N. Kryzhanovskiy, All-Union Scientific Cardiology Center, USSR Academy of Sciences; Institute of General Pathology and Pathological Physiology, USSR Academy of Medical Sciences, Moscow]

[Abstract] Compound SKF 10047 (N-allylnormetazocine) injected in animals induces a series of reactions: psychotic states, ataxia, respiratory depression, dilation of pupils, tachycardia, etc. In the present study, stereoselective, saturable, reversible and temperature-dependent binding of tritiated SKF 10047 to mouse splenocytes was demonstrated. The binding centers for SKF 10047 resemble sigma receptors in mammalian brain as well as binding centers in rat liver membranes. The binding capacity was 100 molecules per cell. The functions of sigma receptors are not clear, but they seem to mediate a number of psychotomimetic reactions in humans and in animals. Figures 2; references 12: 2 Russian, 10 Western.

7813/9604

Hypothalamus Transplants Extend Life in Mice

18400311 Moscow TASS in Russian 31 Mar 88

[Article by TASS correspondent Ivan Ivanov]

[Text] It is possible that man can live for 300 years if a simple operation is performed on his brain. This is suggested by the results of experimentation on animals conducted at the Institute of Evolutionary Morphology and Ecology of Animals of the USSR Academy of Sciences. Ordinary mice have been kept for about 3 years in a cage at a laboratory at the institute. "Geneticists say that the life span of this species is only 2 years," said Doctor of Biology Fatima Ata-Muradova. "But the mice kept in the laboratory have become long-lived after tiny pieces of hypothalamus of new-born mice or of embryos were planted in their brain."

The hypothalamus is the part of the brain that is concerned with important vital functions of the body—metabolic functions—that govern the hormonal and immune systems and many others. "The operation not only 'rejuvenated' the brain but also stimulated the activity of most organs in the animals operated on," Ata-Muradova said. "The mice survived for longer than the animals that have not been operated on and are healthy and lively, and some could even continue breeding. Their immune system has been rejuvenated and was able to protect the body effectively again."

The experiments confirmed the theory that the brain directly affects physiological processes in the body. Ata-Muradova believes that pieces of embryo implanted in the brain of an adult animal impart an additional genetic "program" to its brain. Besides that, experiments showed that the implanted nerve tissues regenerate the neighbouring aged tissues and speed up the growth of cells. The scientist believes that this means the experiment proved a direct dependence of functions of the immune system of the brain. "It can be that with the passage of time people will learn to control their health even by willpower," the scientist suggested.

"It would naturally be premature to make such experiments on humans. The mechanism of the functioning and aging of the brain, of the body as a whole should be understood more profoundly. But while, as scientists believe, man is genetically programmed to live for at least 200 years, his life span can be extended for at least another 100 years," Fatima Ata-Muradova said.

In the conversation with the TASS correspondent the scientist also suggested that it might be possible to treat AIDS (Acquired Immune Deficiency Syndrome) by means of implanting embryonic hypothalamus. If an embryo not affected by the virus is implanted in the brain of an AIDS patient, the protective resources of the body might be activated and functions of the immune system restored. "The same methods can be tried in treating cancer," Dr Ata-Muradova suggested. "I have, though, modest expectations of success, as no one has yet been able to thoroughly explain the phenomenon of the body's protective resources."

/09599

Effect of Delta Sleep-Inducing Peptide on Gamma-Aminobutyric Acid and Glutamate Level and Glutamate Decarboxylase Activity in Rat Brain Sections

18400197b Yerevan NEYROKHIMIYA in Russian Vol 6, No 3, Jul-Sep 87 (manuscript received 20 Mar 87) pp 422-425

[Article by A. M. Mendzheritskiy, M. G. Makletsova and I. Yu. Karpukhina, Scientific Research Institute of Neurocybernetics and Scientific Research Institute of Biology, Rostov State University imeni M. A. Suslov]

[Abstract] The effect of intracisternal injection of delta sleep-inducing peptide [DSIP] on the activity of the γ-aminobutyric acid [GABA] system in rat brain was studied following stereotaxic injection of 15 nmole/kg DSIP into the 3d ventricle of the brain. White male rats weighing 150-170 g were used. Control rats received physiological solution intracisternally. The GABA level, glutamate level and glutamate decarboxlase (GDC) activity were determined 60 minutes after injection of DSIP in the cerebral hemisphere, the midbrain, the afterbrain and the cerebellum. DSIP injection increased the GABA level by 62 percent, the glutamate level by 78 percent and GDC activity by 132 percent. The GABA and glutamate levels and GDC activity in the afterbrain, the cerebellum and the cerebral hemisphere were the same but injection of the peptide increased GABA and glutamate levels in the midbrain somewhat and decreased GDC activity significantly. The study confirmed the hypothesis concerning the possible neuromodulator function of DSIP, realized via the neurotransmitter system. References 15: 12 Russian; 3 Western.

02791

DNA Synthesis and Mitotic Division of Large Hemisphere Cortex Neurons in Adult Rats During Intracranial Transplantation of Embryonal Nerve Tissue, Based on Experimental Autoradiographic Data

18400235a Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 298, No 4, Feb 88 (manuscript received 29 Jun 87) pp 988-990

[Article by L. V. Polezhayev, M. A. Aleksandrova and V. N. Kleshchinov, Institute of General Genetics imeni N. I. Vavilov, USSR Academy of Sciences, Moscow]

[Abstract] Under certain conditions mature brain neurons of birds and mammals may synthesize DNA and divide in vitro and in vivo. The principal condition for this phenomenon is mechanical damage of the brain neuron tissue or administration of neurotropic factor.

This aspect was verified experimentally on Wistar rats: small segments of embryonal brain cortex were implanted in their right hemisphere sensorimotor region followed by i.p. injection of ^{3}H-thymidine 3 days after the implantation. Histological analysis of brain tissue showed intensive incorporation of ^{3}H-thymidine into the cells surrounding the transplant at about the 4th day after the implantation, indicating replicative DNA synthesis in the neuron cells accompanied by mitotic cell division. Thus it was shown that special conditions exist when allotransplanted neurons can take, develop and be preserved for an extended time. This phenomenon occurs at least in some cells which normally do not manifest this activity. The role and fate of such cells remain obscure and require further studies. Figure 1; references 15: 11 Russian, 4 Western.

7813/9604

Distribution Asymmetry of Muscular Tone Peptide Regulators and Substance P in Rat Spinal Cord With Unilateral Hyperactivity of Lumbar Enlargement Neurons

18400234b Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 12, Dec 87 (manuscript received 21 Jul 86) pp 657-660

[Article by G. N. Kryzhanovskiy, V. K. Lutsenko, and M. Yu. Karganov, Laboratory of General Pathology of the Nervous System, Scientific Research Institute of General Pathology and Pathological Physiology, USSR Academy of Sciences, Moscow]

[Abstract] Peptides play an important role in supporting asymmetric changes in spinal cord functions during vestibulopathy. To verify the possibility that this occurs also in other forms of unilateral motor hyperactivity of the spinal cord, experiments were performed on animals in which asymmetry of muscular tonus was evoked by injection of tetanus toxin into the gastrocnemius muscle. This led to relatively stable unilateral hyperactivity of lumbar enlargement neurons. The lumbar enlargement factor, which is thought to consist of peptides, increased the duration of passive hind limb extension after intracisternal injection to healthy animals on the side where the donor animal neurons were hyperactive. Extracts from healthy animals showed no effect. Prencubation of the extract with pronase or coinjection of naloxone (an opiate antagonist) eliminated these unilateral changes. The level of substance P in the spinal cord of the donor was elevated bilaterally, but it was higher in the hyperactive side. References 13: 7 Russian, 6 Western.

7813/9604

Blood Flow in Skin Wound Tissue and Systemic Hemodynamics Resulting From Collagen-Dalargin Complex

18400234a Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 12, Dec 87 (manuscript received 27 Jan 87) pp 651-654

[Article by O. S. Medvedev, G. Ya. Khulup, S. Ye. Spevak, L. P. Istranov, M. I. Titov and A. M. Demetskiy, Institute of Experimental Cardiology, All Union Scientific Cardiology Center, USSR Academy of Medical Sciences, Moscow]

[Abstract] Recently published data showed that opiopeptides are capable of stimulating regenerative processes of many tissues. The effect of dalargin (Tyr-D-Ala-Gly-Phe-Leu-Arg) complexed with collagen on capillary blood flow in skin wounds was studied, and systemic hemodynamic parameters in rats were evaluated at different healing times. The studies were performed with white male Wistar rats. It was shown that dalargin stimulated reparative processes of injured tissue, possibly by activating blood flow in the regenerating tissue. Analysis of the data obtained with radioactive microspheres and by histological and histochemical methods showed that dalargin increased the blood flow in granulation tissue by formation of new capillaries and decrease of the vascular resistance. Dalargin showed no effect on capillary blood flow in unaffected tissues. Figure 1; references 15: 8 Russian, 7 Western.

7813/9604

Dangerous Effects of Preliminary Hyperventilation During Diving

18400248 Moscow TEORIYA I PRAKTIKA FIZICHESKOY KULTURY in Russian No 1, Jan 88 pp 42-44

[Article by T. M. Potapova and A. V. Potapov, All Union Scientific Research Institute of Pulmonology, USSR Ministry of Health]

[Abstract] The goal of this study was to determine the process of the saturation of arterial blood with oxygen during artificial, voluntary apnea under water, after hyperventilation with atmospheric air. Twenty volunteers aged 19-22 years were evaluated. The results showed that preliminary hyperventilation increased the time one can spend under water without breathing both in a state of rest and during physical exercise. It does not prevent the loss of consciousness during diving. This phenomenon occurs suddenly without any warning. New, scientifically based recommendations need to be developed regarding the type and duration of hyperventilation preceeding diving exercises. References 14: 5 Russian, 9 Western.

7813/9604

Use of Computers in Processing Functional Diagnostic Data

18400249 Minsk ZDRAVOOKHRANENIYE BELORUSSII in Russian No 1, Jan 88 (manuscript received 21 Apr 87) pp 51-54

[Article by V. A. Lollini and N. I. Stepanenko, Department of Therapy (headed by A. N. Okorokov), Department for Advanced Training of Physicians, Vitebsk Medical Institute; Division of Public Health, Executive Committee of Vitebsk Oblast Soviet of National Deputies]

[Abstract] An automated system for processing clinical data was developed and used in practical application at the Vitebsk Regional Hospital, Department of Functional Diagnosis. The principal functions of this system are: automated registry, processing and storage of graphic information obtained in studies of cardiovascular and pulmonary systems. All components of this system are produced domestically. Thus far data from 673 patients were entered into this system, which stores hundreds of rheograms and shows reliable performance and improved accuracy in processing clinical information. In spite of this obvious success, wide application of this system is sporadic at best, mainly due to the resistance of individual physicians who need to be thoroughly indoctrinated in the advantages of this modern technique. References 15: 8 Russian, 7 Western.

7813/9604

Mathematical Simulation of Psychophysiological Characteristics

18400198a Moscow PSIKHOLOGICHESKIY ZHURNAL in Russian Vol 8, No 6, Nov-Dec 87 pp 48-56

[Article by V. F. Prisnyakov and L. M. Prisnyakova, Dnepropetrovsk State University]

[Abstract] Functions for calculating the short-term memory span and the latent period of operator reaction and for determining the relationship between stimulation and perception were obtained on the basis of the authors' mathematical model of information processing by the memory. The effect of an alphabet of signals and the rate of feed of information on the memory span was analyzed. It was shown that the theoretical formula for determining human reaction time includes well-known empirical formulas. Analysis and comparison of theoretical results were compared with experimental data from other authors. Figures 3; references 12: 11 Russian; 1 Western.

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Autohypnotraining (Method of Mental Self Regulation)

18400198b Moscow PSIKHOLOGICHESKIY ZHURNAL in Russian Vol 8, No 6, Nov-Dec 87 pp 105-109

[Article by V. I. Natarov, Northwestern Polytechnical Correspondence Institute]

[Abstract] A modified method of mental self-regulation, autohypnotraining, which includes elements of hypnosis and autogenic training with the use of tape recordings, was described and discussed. A training method was described and results of practical use of the method were presented. Modifying the course of training according to the individual characteristics of persons involved improves the effectiveness of the method. Any modification of autohypnotraining involves 5 components: conviction, suggestion, psychological state of relaxation, relationship between the state of the muscle system and the emotions and means of mediated regulation of activity of the internal organs. The method was recommended for use by mental hygienists and psychotherapists and may prove to be useful to persons working under extreme conditions. References 19: 14 Russian; 5 Western.

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Effective Method for Plasmid DNA Incorporation into Eukaryotic Cells Using Liposomes in the Production of Vaccinia Virus Recombinants

18400195d Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104, No 10, Oct 87 (manuscript received 12 Oct 86) pp 478-480

[Article by V. A. Slepushkin and M. I. Bukrinskiy, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Sciences; Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamalaya, USSR Academy of Medical Sciences, Moscow]

[Abstract] Vaccinia vaccine has been used extensively as a vector for cloning allogenic genes because of the high capacity of this vector and the wide spectrum of recipient cells which are sensitive to the virus. Recently, liposomes containing viral or plasmid DNA began to be used for transformation of eukaryotic cells. In this study an effective method is proposed for introducing plasmid DNA into a cell via inducement, with the aid of ultraviolet-radiation inactivated Sendai virus, of fusion of ganglioside-containing liposome membranes with the cellular plasma membrane. This method was used to produce recombinant vaccinia virus carrying the env gene of HTLV-3/LAV virus. The data indicated the high effectiveness of liposomal DNA penetration into the cell and its subsequent recombination with vaccinia virus DNA. The method was used successfully to produce recombinant vaccinia virus carrying a fragment of the env gene of the AIDS virus. Fig. 1: references 15 (Western).

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Dhori Virus, a Human Pathogen. Five Cases of Infection of Laboratory Workers

18400208a Moscow VOPROSY VIRUSOLOGII in Russian No 6, Nov-Dec 8 (manuscript received 12 Aug 86) pp 724-729

[Article by A. M. Butenko, Ye. V. Leshchinskaya, I. V. Semashko, M. A. Donets, L. I. Martyanova, I. N. Martynenko, S. G. Rubin and M. P. Chumakov, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences; Institute of Poliomyelitis and Virus Encephalites, USSR Academy of Medical Sciences, Moscow]

[Abstract] Dhori virus, one of a group of arboviruses ecologically associated with Ixodidae ticks, was first isolated in India in 1961 from Hyalomma dromedarii ticks and then from Hyalomma dromedarii ticks in Egypt and repeatedly from different Ixodidae ticks collected in the USSR in Astrakhan Oblast, Krasnodarsk Kray, Armenia and Azerbaijan and also in Portugal. Dhori virus strains isolated in the USSR and India (prototype strain 611313) have been studied at the hemorrhagic fever laboratory of the Institute of Poliomyelitis, USSR Academy of Sciences, for the last 14 years without any cases of disease for 12 years. In 1978 and 1979, 2 scientists and 3 laboratory workers engaged in this study contracted disease caused by Dhori virus. Two cases discovered in June and July 1978 involved work with strain 611313, and 3 cases occurring in March-April 1979 were attributed to the Pyatnitskaya strain of Dhori virus, isolated from blood of a patient infected in 1978. This article describes the clinical picture of these cases and presents results of virological and serological studies which established, for the first time, the pathogenicity of Dhori virus for man. The infection of five out of six persons who worked with the virus showed its high contagiousness. Clinical infection by the virus was characterized by an acute course with pronounced general intoxication and a rather brief (2-4 days) febrile period. Two of the patients suffered changes in the nervous system of the type of encephalitic reaction with predominance of subcortical symptoms and slight involvement of the pyrimidal system or in the form of encephalopolyradiculoneuritis with paresthesia and sensitivity disorders. Both clinical and encephalographic symptoms regressed within 2-3 weeks without apparent aftereffects. The asthenic syndrome persisted for 45-60 days in all 5 patients. Some aspects of differential diagnosis of Dhori virus infection were discussed briefly. References 10: 5 Russian; 5 Western.

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Development and Basic Properties of Virus Preparation Viroden

18400208b Moscow VOPROSY VIRUSOLOGII in Russian No 6, Nov-Dec 87, (manuscript received 26 Feb 86) pp 729-733

[Article by L. P. Buchatskiy, M. A. Kuznetsova, N. N. Lebedinets and A. G. Kononko, State University imeni T. G. Shevchenko, Kiev]

[Abstract] A virus preparation, viroden, the active ingredient of which is the densonucleosis virus of blood-sucking mosquitoes, strain GKV-002002, belonging to the Parvoviridae family, was developed and tested for its effectiveness in controlling blood-sucking mosquitoes of the Aedes, Culex and Culiseta genera. The preparation was effective against mosquitoes in the pre-imago stage and against flying mosquitoes. Mortality at the pre-imago stage was 77 percent, while only 15.4 percent survived up to the first female gonadotrophic cycle. The overall effectiveness of viroden was 84.6 percent compared to a 10-18 percent mortality in the control group. The preparation remained stable during storage and remained effective after exposure to solar radiation and heat and after changes of pH without significant loss of potency. The preparation has narrow specificity and apparently affects only Aedes, Culex and Culiseta mosquitoes. Further tests of viroden in different climatic

zones were recommended. References 21: 9 Russian; 12 Western.

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Fourth All-Union Seminar-Conference on Molecular Genetics of Yeasts (Old Petrograf, Leningrad, 1-5 June 1987)

18400194b BIOTEKHNOLOGIYA in Russian Vol 3, No 6, Nov-Dec 87 (manuscript received 29 Jun 87) pp 809-812

[Article by Yu. O. Chernov, I. I. Tolstorukov and M. Yu. Beburov, Department of Genetics and Selection, Leningrad State University imeni A. A. Zhdanov; All-Union Scientific Research Institute of Genetics, Moscow; All-Union Scientific Research Institute of Biotechnology, Moscow]

[Abstract] Soviet scientists have held respected positions in the international community of yeast genetics in some areas such as genetic control of translation, genetics of life cycles, the mutation process and regulation of some pathways of metabolism. However, in the 1970s, in the period of rapid development of the genetics of yeasts in the West, and especially after its transition to the molecular level and the birth of gene engineering, Soviet scientists fell behind. There was an obvious need for informal exchange of experience, discussion of ongoing research and availability of extensive general information. These conditions inspired the idea of conducting All-Union conferences on the genetics of yeasts. The scientific program of the fourth seminar-conference included 13 lectures on vital problems of the genetics of yeasts, 2 sessions on innovations in molecular genetics of yeasts and 3 round tables with participants discussing their own experiments and developments. Most reports were devoted to the organization of the yeast genome. Much attention was given to the problem of regulation of the action of the gene at different levels and biotechnology problems associated with this. The use of regulatory segments of DNA to construct vector plasmids which ensure high and/or regulated expression of allogenic genes in yeasts was discussed in some detail. In all presentations at the round table, special attention was given to using a potent yeast promotor and ensuring the secretion of the product into the medium. The conference confirmed the significant progress in genetic regulation and gene engineering biotechnology in the Soviet Union.

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Seventh All-Union Symposium on Search for Physiologically Active Substances

18400217 Riga KHIMIYA GETEROTSIKLICHESKIKH SOYEDINENIY in Russian No 10, Oct 87 pp 1425-1426

[Article by G. Ya. Dubur]

[Abstract] About 250 scientists from 20 cities in the USSR attended the symposium, conducted in Yurmal (LaSSR) on January 26-29, 1987, and presented 26 papers concerning problems of synthesis of physiological active compounds. E. Ya. Lukevitsa (Institute of Organic Synthesis, LaSSR Academy of Sciences) showed that silyl methods are suitable for laboratory and industrial synthesis of various medicines, including heterocyclic compounds. V. P. Mamayev and O. A. Zagulyayeva (Novosibirsk Institute of Organic Chemistry, USSR Academy of Sciences, Siberian Department) discussed new methods of synthesis in the chemistry of pyrimidines and the effect of compound structure on the reaction capacity. M. Yu. Lidak (Institute of Organic Synthesis, LaSSR Institute of Organic Synthesis) discussed the prospects of use of derivatives and analogs of nucleosides and nucleotide bases in prevention and treatment of malignant tumors. D. G. Knorre (Institute of Bioorganic Chemistry, USSR Academy of Sciences, Siberian Department) discussed effective and automatic methods of chemical synthesis of oligonucleotides. K. M. Dyumayev and L. D. Smirnov, (Scientific Research Institute of Pharmacology, USSR) discussed studies of 3-hydroxypyrimidines and 5-hydroxypyrimidines. Ye. B. Burlakova (Institute of Chemical Physics, USSR Academy of Sciences) discussed the role of endogenous and exogenous antioxidants in the regulation of antioxidative activity in the cell. S. Ye. Severin (Moscow State University) discussed some natural antioxidants which can be used in treatment of cataracts. Yu. A. Vladimirov (2d Moscow Medical Institute) discussed antioxidants which prevent cataracts. S. A. Andronati (Physicochemical Institute, UkSSR Academy of Sciences) described the role of receptor-ionophore complexes of benzodiazepines in creating new biologically active substances. Achievements in synthesizing heterocyclic and carbocyclic analogs of prostaglandins were discussed by K. K. Pivnitskiy (Institute of Experimental Endocrinology and Chemistry of Hormones, USSR Academy of Medical Sciences). L. D. Bergelson and V. V. Bezuglov (Institute of Bioorganic Chemistry, USSR Academy of Sciences) discussed achievements in selective halogenation of prostaglandins. Ya. P. Stradyn (Institute of Organic Synthesis, LaSSR Academy of Sciences) discussed the combined use of different physical and physicochemical methods to establish the structure of heterocyclic and other organic substances. S. M. Navashin and Yu. O. Sazykin (All-Union Scientific Research Institute of Antibiotics) described means of creating new antibiotics with the use of organic synthesis and biotechnology.

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